Derivation of New ICM-stage hESCs

Grant Award Details

Derivation of New ICM-stage hESCs

Grant Type: New Cell Lines

Grant Number: RL1-00642-A

Investigator:

Name:	Sheng Ding
Institution:	Scripps Research Institute
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell, Other

Cell Line Generation: Embryonic Stem Cell, iPS Cell, Other

Award Value: $936,973

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Grant Application Details

Application Title: Derivation of New ICM-stage hESCs

Public Abstract: Recent studies in the derivation of rodent pluripotent epiblast stem cells and their molecular characterizations have provided strong evidence that the conventional human embryonic stem cells may represent a distinct, later developmental stage, i.e. late epiblast stage, than the conventional murine embryonic stem cells, which is a “capture” of the ICM stage. Those two stages (i.e. ICM/pre-implantation stage vs. epiblast/post-implantation stage) of pluripotent stem cells are typically maintained in their self-renewal state by different sets of exogenous signaling molecules. Meanwhile, other studies have suggested that rather than exogenously activating multiple additional pathways to achieve a fine balanced self-renewal state, a more fundamental approach to main self-renewal of stem cells is to inhibit endogenously expressed differentiation-inducing protein activity. In addition, cell-permeable small molecules have the unique advantage of acting intracellularly to inhibit differentiation without requirement of expression of the desirable membrane receptors by cells for transducing differentiation-inhibiting signals by the desirable exogenous growth factors in the culture media. Those studies together suggested the possibility that an earlier stage (i.e. ICM-stage) of human pluripotent stem cells than the conventional human embryonic stem cells, which would represent an equivalent counterpart of the conventional murine embryonic stem cells, could be derived with helps of small molecules that could block further differentiation and capture the state of human ICM-stage of pluripotent stem cells. Here we propose to screen chemical libraries for small molecules that can facilitate derivation of the above hypothesized, new, earlier developmental state of human pluripotent stem cells from donated human IVF blastocysts. Such new human pluripotent stem cells may have better properties than the conventional human embryonic stem cells (e.g. ease of culture and manipulation), facilitate ready transfer of knowledge/techniques learn from murine embryonic stem cells to human pluripotent stem cells, and perhaps provide a new cell type for studying fundamental biology.

Statement of Benefit to California: The putative human pluripotent stem cells proposed here may have better properties than the conventional human embryonic stem cells (e.g. ease of culture and manipulation), facilitate ready transfer of knowledge/techniques learn from murine embryonic stem cells to human pluripotent stem cells, and perhaps provide a new cell type for studying fundamental biology. In addition, small molecules have been more useful than genetic approaches in the treatment of human disease. The demonstration that one can systematically identify, optimize and characterize the mechanism of action of small drug-like molecules that selectively control cell fate and reprogramming will: (1) provide important tools to manipulate cell fate in the lab; (2) provide new insights into the complex biology that regulates (stem) cell fate; and (3) provide an important first step which may ultimately lead to drugs that facilitate the clinical application of stem cells.
